PREDICTORS OF PERIOPERATIVE OUTCOME AFTER HEPATECTOMY: A PROSPECTIVE ANALYSIS

Dissertation

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<u>CERTIFICATE</u>

This is to certify that the Dissertation titled **"PREDICTORS OF PERIOPERATIVE OUTCOME AFTER HEPATECTOMY: A PROSPECTIVE ANALYSIS"** of **Dr V. VIMALRAJ** is done in partial fulfillment of the requirements of M.Ch. Branch VI Surgical Gastroenterology Degree Examination of The Tamilnadu Dr. M.G.R. Medical University to be held in August 2007. The period of study is from August 2004 to August 2007.

Head of the Department,
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DEAN

DECLARATION

I, **Dr. V.Vimalraj**, solemnly declare that dissertation titled, **"PREDICTORS OF PERIOPERATIVE OUTCOME AFTER HEPATECTOMY: A PROSPECTIVE ANALYSIS"** is the bonafide work done by me at Govt. Stanley Medical College and Hospital during the period August 2004 to March 2007 under the expert guidance and supervision of **Prof. R. Surendran, M.S., M.N.A.M.S., M.Ch, Head of the Department,** Department of Surgical Gastroenterology.

The dissertation is submitted to the **Tamil Nadu Dr. MGR Medical University** towards partial fulfillment of requirement for the award of **M.Ch Degree (Branch VI) in Surgical Gastroenterology**.

Place : Chennai

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CONTENT

INTRODUCTION

Evolution of surgical techniques in partial hepatectomy has enabled the procedure to be performed with operative mortality rate of less than 5% in high-volume centers in recent years.[1–5] Before the 1980s, hepatic resection was typically associated with a mortality rate of greater than 10%.[6–9] Better understanding of the segmental liver anatomy and refined surgical techniques in controlling hemorrhage are the 2 most important factors that have contributed to the improved perioperative outcome of hepatectomy.[5,10] Another important factor is the better selection of patients in terms of liver function reserve and comorbid conditions, which helps to reduce mortality from liver failure and other severe postoperative complications such as pneumonia.[3,11,12] Finally, the concentration of hepatic resection in experienced hepatobiliary centers is also a critical factor. Recent studies from other countries have demonstrated that a high hospital mortality rate of around 10% is still being observed in low-volume hospitals, whereas the hospital mortality rate in high-volume centers is less than 5%[13,14].The improved safety of hepatic resection has led to the broadening of the indications of hepatectomy in patients with normal liver.[3,4] partial hepatectomy in combination with other major procedures is now performed with greater frequency.

Partial hepatectomy is now performed more frequently in good-risk patients with conditions associated with normal liver, such as colorectal liver metastasis.[15] The improved safety of hepatic resection has also led to a more liberal application of the procedure in patients with benign tumors.[16] With the enhanced safety, some surgeons have advocated hepatic resection for some noncolorectal liver metastases even though the oncological benefit remains unclear. [17,18] However, the role of hepatic resection in patients with chronic liver disease is still considered limited because of the associated increase in operative mortality and morbidity, especially when major hepatic resection is required. [14,19,20] Advanced age is considered another limiting factor as several recent studies have reported that elderly patients had significantly increased operative morbidity and mortality.[4,14,20] It remains to be demonstrated that the role of hepatic resection can be extended to such high-risk patients with favorable perioperative outcome. The practice of hepatic resectional surgery thus continues to evolve, but few large, contemporary studies have specifically evaluated the impact of these changes.[21] The present study analyzes consecutive, unselected patients undergoing hepatic resection over the past three years to further define factors associated with morbidity and mortality and to evaluate trends in operative and perioperative variables over the period of study.

AIMS AND OBJECTIVES

The current study aims to analyze the trends in perioperative outcome of 40 consecutive patients with hepatectomy for various benign or malignant hepatobiliary diseases in a specialized hepatobiliary center over a period between August 2004 and March 2007, with a particular reference to the prevalence of underlying risk conditions such as impaired liver function reserve, advanced age, and presence of comorbid illnesses.

REVIEW OF LITERATURE

Liver surgery has a recent history compared to other branches of surgery which evolved gradually, achieving technical standardization and worldwide adoption many decades earlier. The modern era of liver surgery dates just 50 years, when the intra hepatic segmental anatomy was classified. Progress from pioneering to routine surgery is even more recent, corresponding to the advent of ultrasonography and improvements in diagnostic and interventional radiology over the past 30 years. Resectional surgery has undoubtedly benefited from the experience gained both in anesthesia and perioperative and post operative care of the liver transplant patients.

For the surgeon, the importance of precise knowledge of the hepatic anatomy and its variants is perhaps no where more apparent than in hepatic surgery. Detailed anatomical studies, particularly works of Glisson, Cantlie, Couinaud, Goldsmith and Woodburne have defined the segmental anatomy that is essential for hepatectomies. The anatomical division between the right and left lobes follows a line projected through a plane (the principal plane or Cantlie line) running from the medial margin of the gallbladder bed to the IVC posteriorly. Each major right and left portion of the liver is further subdivided in to sectors and segments. Between the sectors, the draining hepatic veins converge posteriorly towards the vena cava and mark the main scissura of the liver. Each segment is supplied by a portal triad.

Patient Assessment

Medical evaluation is done as for any major upper abdominal surgery. Pulmonary complications are particularly common after liver resection because of a high transverse incision is always accompanied significant incisional discomfort. The sympathetic right pleural effusion that is uniformly present after liver resection further compromises the respiratory function. Patients with preexisting cardiac conditions are also at an added risk. Patients with parenchymal disease should be specifically assessed for gas exchange impairment, alcoholic or nutritional associated cardiomyopathy, infection, decompensation due to cirrhosis, acute alcoholic hepatitis and renal impairment. Advanced chronological age is no longer a contraindication to surgery.

Assessment of the Liver

Liver resections are increasingly performed as a standard treatment of various hepatobiliary diseases. However, there were few contemporary studies of the perioperative outcome of hepatic resection.[3-5] In a study of 747 hepatectomies by Belghiti et al[3] demonstrated a operative mortality of 1% in patients with normal liver, but the operative mortality rate was 8.7% in cirrhotic patients. Jarnagin et al[4] reported a series of 1803 patients with hepatic resection and demonstrated a significant improvement in the perioperative outcome over the study period, which was attributed to the increased use of parenchymal preserving segmental resections and decrease in the number of hepatic segments resected. More recently Imamura et al reported zero mortality after hepatic resection in a series of 915 patients. The authors emphasized the importance of case selection, and they adopted a strict selection in terms of liver function reserve.

Assessment of liver function is a critically important tool for selecting patients for hepatic surgery. Not only is it important in the assessment of a patient's ability to withstand resection, it also has clearly played a role in the selection process that surgeons apply to individual patients in tailoring the appropriate extent of resection. These decisions are based on the requirement for adequate margins of resection, balanced against any underlying hepatic functional impairment that tends to limit the safe extent of resection.

In recent years, the assessment of liver function has had an increasingly important role, as surgeons attempt to overcome the limits of anatomic constraints and the volume of tumor to increase resection rates. For it must not be forgotten that surgical resection remains the mainstay of cure for patients with hepatic malignancies, and no effort to achieve resection should go unexplored. The importance of assessing liver function has been further increased because the goal of several aggressive preoperative therapies designed to improve the liver functional reserve before resection requires some means of assessing whether, in fact, functional reserve has been improved. Successful liver resection for primary or metastatic liver tumors involves the surgeon's recognition that hepatic regeneration will occur, and that this metabolic demand is superimposed on the necessary homeostatic functions of the liver. Postoperative tolerance of resection and the ability to regenerate the missing parenchyma are markedly different among patients. The generally acknowledged equivalency of limited versus major lobar and extended resections has, in a sense, been an implied recognition of the limitations on resection imposed by such conditions as cirrhosis.

What is hepatic reserve? – the surgeon’s concept over the years, experienced hepatobiliary surgeons have developed selection criteria that allow them to avoid or to limit liver resection in patients whose ability to tolerate resection appears impaired. In part, this decision process has been aided by clinical classification systems such as the Child classification scheme and various liver-function tests. Despite these tools, it is surprising to some clinicians that liver failure remains a significant contributor to postoperative morbidity and mortality. By the same token, experienced hepatic surgeons have a remarkable ability to match patients to an appropriate operation, thus achieving maximal benefit with low risk.

In Table 1, several series are reviewed in which the overall liver failure rate leading to death ranges from 2% to 65% following hepatic resection for hepatocellular carcinoma (HCC). Patients who have HCC often have underlying cirrhosis as an etiologic factor for their tumors; thus liver failure as a cause of postoperative mortality is not surprising in this group. What is often more surprising, however, is that liver failure is a substantial component of mortality after liver resection for colorectal cancer. Table 2 indicates that mortality rates after resection for colorectal cancer have a wide range, with up to 50% of deaths stemming from liver failure. Prolonged recovery and even late deaths can also occur for this same reason, further indicating the importance of liver reserve in recovery from hepatic surgery.

Table 1

Liver Failure after hepatic resection: hepatocellular carcinoma

	No. Patients	**Deaths**	**Deaths due to liver failure (%)**
Kanematsu et al [85]	50	4 (limited)	1 (25%)
		2 (lobar)	1 (50%)
Lee et al [86]	109	6	3 (50%)
Nagasue et al [54]	118	9	5 (55%)
Nagao et al [53]	99	19	8 (42%)
Tsao et al [87]	322	48	32 (65%)
Arii et al [88]	3395	2–25%	
Nonami et al [89]	262	27	27 (100%)

Table 2

Liver failure after hepatic resection: colorectal cancer metastases

	No. Patients	Deaths	Deaths due to liver failure (%)
Fortner [95]	65	6	3 (50%)
Iwatsuki [96]	48	1	0
Ekberg et al [90]	81	4	2 (50%)
Nordlinger et al [91]	80	4	2 (50%)
Doci et al [92]	100	5	0
Doci et al [93]	208	5	2 (40%)
Nordlinger et al [94]	1568	36 (2.3%)	6 (16%)

What then is hepatic reserve? Moving beyond the financial analogy, hepatic reserve is the combined functions of the liver as determined by hepatic parenchyma, the reticuloendothelial system, unique cells in the liver (ie, Ito cells), and hepatic blood flow, including major arterial, portal venous, hepatic venous; and microvascular blood flow in the spaces of Disse. Preservation of parenchymal volume appears to be under the complex control of a number of factors derived from the portal venous circulation, including insulin and hepatocyte growth factors among others. The functions of the liver are varied and some are quite complex. A simplistic summary of liver function includes the synthesis and degradation of glucose and glycogen, fatty acid metabolism, and the synthesis of a variety of proteins, as well as detoxification of lipid soluble toxins, degradation of bilirubin, and the general degradation of serum proteins targeted for routine turnover.

The clinical assessment of hepatic function has evolved from the Child system, developed to understand the significance of cirrhotic liver injury and portal hypertension as they related to patient survival and surgical outcomes for portal-systemic shunt surgery [48]. This system has also been applied to determine mortality estimates for elective operations, and as a means to follow the clinical course of patients with liver disease, in an effort to recognize changes that require alterations in therapeutic strategy.

The original Child system assessed the degree of ascites, the presence and severity of encephalopathy, and the levels of bilirubin and albumin (Table 3)[49]. Recent modifications of the Child assessment have included the Pugh modification, which includes the prothrombin time (or international normalized ratio (INR)) and does not look at nutritional status, except indirectly via plasma albumin levels[50]. In another modification, the Child-Campbell system, a scoring system similar to that of Child-Pugh (CP) is used—presence and degree of ascites, encephalopathy, bilirubin, and albumin, and nutritional status are considered. By replacing the evaluation of prothrombin time or INR with nutrition assessment, the Child-Campbell score can be obtained in locales without the ability to obtain those coagulation tests[51]. Less widely applied alternatives to the CP and Child-Campbell scores include the Apache III scoring system, and ANS, or ascites/nutritional score. The CP score has widest use among surgeons. This has been facilitated by its simple scoring system (Table 4)[50, 51].

Table 3

Hepatic function assessment using the Child system and its modifications

Variable	Child	Pugh	Campbell
Ascites	X	X	X
Nutrition			X
Encephalopathy	X	X	X
Bilirubin	X	X	X
Albumin	X	X	X
Protime/international normalized ratio (INR)		X	

Table 4

Child-Pugh scoring system

[a] Child-Pugh Class A, 5–6 total points; Child-Pugh Class B, 7–9 total points; Child-Pugh Class C, 10–15 total points.			
Points	**1**	**2**	**3**
Ascites	None	diuretic controlled	Tense
Encephalopathy	Absent	State I–II	State III–IV
Albumin (g/L)	>3.5	2.8–3.5	<2.8,
Bilirubin (mg/dL)	<2	2–3	>3
PT(sec above control), or	<4	4–6	>6
INR	<1.7	1.7–2.3	>2.3

How useful are these clinical systems? How is general survival equated with the A, B, and C stratification resulting from the Child classification and its refinements? What has been the predictive value of these systems? And, particularly, how well do these classification schemes predict outcomes in liver resection? Are they useful for defining the limits of resection; that is, the limits of hepatic reserve?

In the CP system, a score of 5 to 6 garners a Child A classification. Patients in this stratum generally would be presumed to have virtually no risk for mortality from liver-related causes during the subsequent year. With increasing debility, scores of 7 to 9 merit a classification of B, and these cirrhotic patients carry a 20% risk of 1-year mortality from liver-related complications of cirrhosis such as variceal bleeding and hepatic failure. A CP score of 10 to 15 out of a total score possible score of 15 merits a C classification. Such patients bear a 55% 1-year mortality risk, again stemming from complications of cirrhosis such as gastrointestinal bleeding and hepatic encephalopathy. Patients classified as B or C become eligible for liver transplant evaluation.

In the Campbell system (substituting nutritional status for prothrombin time), cooperative group data from the Euricterus database demonstrated that only 5% of 1015 cirrhotics would merit classification by Child's criteria[51]. With the Campbell modification, 19% could be classified as Child Class A, and 46% could be classified as Child Class B. Their data also demonstrated that the Pugh's modified Child score, and even the ANS system, also refine the risk estimates for early stage cirrhosis, and therefore may be presumed to provide a better prediction of complications or death from hepatic failure. One would assume that this would apply to surgical risk, as well.

Unfortunately, the predictive value of the Child score for liver resections has been shown to be quite variable. Franco et al[52], for example, demonstrated that the mortality for a Child Class A patient undergoing liver resection was 3.7%, versus 16.7% for both Child Class B and C patients, despite the fact that limited resections were employed. Nagao et al and Nagasue et al demonstrated no differences in mortality based on Child's stratification[53, 54]. Bismuth et al, attempting to use a modified stratification system to predict the limits of resection by stage, reported some success, yet noted five deaths in his series, including those of three early-stage cirrhotic patients who had marginal amounts of liver resected and who by preoperative prediction should have survived[55].

Most hepatic surgeons have discovered that the CP scoring system provides refined predictions of risk compared with the Child scheme; however, there is a persisting unreliability of even the CP score with regard to the Child Class A patients (CP score 5–6). For this reason, hepatic surgeons have pursued laboratory and imaging measures to bolster their clinical assessments and to provide objective data to bolster clinical judgments of patient risk from impaired hepatic reserve. In essence, there is a need to identify “good risk” Child-Pugh A patients and “poor risk” Child-Pugh A patients.

Laboratory and imaging studies to augment Child-Pugh assessment

To overcome the limitations of the CP score for predicting risk of liver failure in patients who are to undergo hepatic surgery, various biochemical tests and imaging studies designed to assess some specific aspect of liver function have been employed to assist in the assessment. These include a variety of single laboratory tests, clearance and tolerance tests, functional imaging, and volumetric tests based on radiological imaging, some of which are listed in Box 1.

Box 1 Various tests of liver function used to assess hepatic reserve

Clearance/tolerance tests

Aminopyrine breath test

Indocyanine green (ICG) retention (clearance)

Bromosulpthalein (BSP) retention

Galactose tolerance

Bile acid tolerance

Beta-hydroxy butyrate/acetoacetate

Functional imaging and blood flow: uptake/clearance

Reticuloendothelium

Gold

Sulfur colloid

Biliary excretion

Rose Bengal

Hepatic diacetic acid (HIDA)

Receptor targeting

Neogalactosyl albumin (NGA)

Galactosyl serum albumin (GSA)

The ideal function test has yet to be invented. The complexity of liver function is such that this is no surprise; however, a successful liver function test, to assist with preoperative assessment of liver function should be safe, reproducible, and easily performed in an outpatient setting. From the busy surgeon's standpoint, the best test is one that can be performed by colleagues or ancillary staff with the time and facilities to achieve these characteristics. Unfortunately, ease of performance is often linked to analyses intended to simplify the complex results for ease of interpretation. The resulting oversimplification of the analysis may reduce the utility of the tests.

How useful have these tests been in predicting surgical outcome? Clearly the tests employed have been employed because of their ease of application. No single test appears to account for the variability of clinical resection results, and, as will be demonstrated, at this point in time no existing test has proven better than the CP system for assessing hepatic functional reserve.

There is no single laboratory test capable of providing this information. Clearance and tolerance tests, however, offer seemingly attractive means to augment the CP assessment (see Box 1). Of these, the most widely used is indocyanine green (ICG) retention. ICG retention is worth focusing on because of its clear selection as the most popular augmentative test used to select patients for resection following CP scoring.

Indocyanine green retention

ICG is a tricarbocyanine dye that binds to albumin and alpha-1 lipoproteins. Its active transfer into the liver parenchymal cells leads to a rapid disappearance from the plasma, and it appears to be solely removed by the liver [56]. From the parenchymal cell, it is secreted into the bile in much the same way as an earlier function test dye, bromsulpthalein[57]. The surgical community has generally opted for the retention time at 15 minutes as a single test—ICG 15. This can be determined by serum sampling, or, as described recently, the percent retention can be determined by pulsed spectrophotometry, using an optical sensor placed on the finger in a similar fashion to an oxygen saturation monitor [58].

In more detailed investigations, several serum values are used to obtain a number of time points to generate a rate-constant, indicating the rate at which the dye disappears from the serum. In this fashion, it has been determined that, rather than being a true index of parenchymal function, there is a substantial influence of hepatic blood flow—both total hepatic blood flow and unit-by-unit flow within the hepatic parenchyma—on the retention of the dye[57]. Hepatic artery vasodilatation may markedly influence the value in the same patient, even on the same day. There is general agreement on the retention values that support major liver resection. Clearance is considered to be impaired when 15% or more of the dye remains within the plasma 15 minutes following the injection of 0.5 mg/kg ICG. Thus, patients with CP scores of 5 or 6 (Child A) and ICG 15 of greater than 14% are the “bad risk” CP A patients whose functional reserve is limited. ICG 15 correlates strongly with CP scores. It also correlates strongly with the rate of disappearance of tagged asialoglycoproteins[59.]

In two important papers assessing the technique of portal vein embolization-improving hepatic functional reserve, Wakabayashi et al and Nakano et al correlated ICG values with hepatic hypertrophy of the contralateral lobe after portal vein embolization[60, 61]. The ICG disappearance rate generally worsened (in 16 of 19 patients) at 2 weeks following treatment. Wakabayashi et al noted that ICG retention was prolonged in a number of patients who subsequently died, but that numerous patients underwent resection without mortality, even in the face of elevated or prolonged ICG clearance. Interestingly, the ICG retention rate worsened in virtually all patients following portal vein embolization at 2 weeks, increasing from a mean of 15.9±6.27% to 20.8±5.6% at 2 weeks. Either 2 weeks is too early to see improved ICG return to baseline clearance, or the altered blood flow due to portal vein embolization results in ICG 15 retention values that do not permit an estimate of hepatocyte function. There is only weak evidence that this test can be useful in assessing the successful accomplishment of liver resection, and lack of correlation is well described[60,62]. Furthermore, the variability of the results depending on total hepatic blood flow, and regional variations can markedly alter the retention value. This reconfirms the information, available as early as 1989, that no quantitative liver function test provided a clear advantage beyond the CP score for predicting outcome in cirrhosis[63]. There have always been strong correlations of the tests with the CP score, but none, including ICG retention, has been directly correlated with outcome.

99m-Tc-galactosyl-human serum albumin scintigraphy

Nuclear imaging with a variety of agents has existed for years, including sulfur and gold colloid scans, and uptake and excretion of Rose Bengal and HIDA. These scanning agents assessed the reticuloendothelial uptake of colloid and the biliary excretion of HIDA. A more recent functional imaging technique with great promise involves receptor targeting with radiolabeled synthetic asialoglycoproteins. In 1966, an active transport process involving the endocytotic removal of senescent serum glycoproteins, which were desialated to allow them to be identified and removed from the circulation by the hepatic parenchyma, was described by Ashwell[64]. Taking advantage of the role of the liver in metabolizing senescent proteins through an active transport process facilitated by hepatocyte membrane receptors, the potential for using this is a liver scanning agent was proposed by Eckelman et al[65] , and a synthetic asialoglycoprotein, galactosyl-neoglycoalbumin (NGA), was complexed to 99m-Tc to study hepatocyte binding via the asialoglycoprotein receptor [66-68]. In addition, imaging provided volumetric/anatomic information, as well as a functional assessment of the ability of the liver to clear the synthetic asialoglycoproteins. Kudo et al, in 1991, reported the development of a similar synthetic asialoglycoprotein, galactosyl human serum albumin (GSA)[69]. This has subsequently been approved for use as a liver-scanning agent in Japan (Nihon Mediphysics, Nishinomiya, Japan), although its use in the United States remains investigational.

Patients undergoing a GSA study receive a bolus injection of 185 MBq 99m-Tc-GSA. A dynamic scintigraph is obtained with gamma cameras located over the heart and liver. The data can then be acquired as planar and single photon emission computed tomographic images. In an effort to simplify interpretation of the data, particularly with regard to proposed surgical use, most investigators have chosen to use the L15 value as an overall estimate of hepatocyte asialoglycoprotein receptor number. Thus the data can be acquired to indicate both the rate of uptake into the liver (or disappearance from the blood pool) and the total number of receptors available. For estimates of postoperative receptor volume, either SPECT images from the GSA scintigraph or CT estimates of the estimated remaining volume of a resection could be used to predict the total number of receptors remaining. The first summary of the US clinical experience with the asialoglycoprotein analog, NGA, demonstrated the correlation of NGA with the CP score, the aminopyrine breath test, and ICG retention [67]. Whether the test provided specific, unique, adjunctive information was not certain. Verification of these data followed with the Japanese analog, GSA, correlating this not only with the ICG retention at 15 minutes, but also with the index of cirrhosis scores, whereas the ICG retention had no correlation with the histologic scores indicating extent of necrosis and fibrosis in patients with chronic active hepatitis[70].

A follow-up article by Kwon et al used technetium GSA to correlate ICG retention and GSA functional imaging[69,71]. This suggested that there is an absolute receptor number below which extended liver resection could not be performed. In their series of 90 patients, however, there were only two operative deaths, one in a low-risk group, and one a patient with marked discrepancy between the GSA and the ICG. In a patient with chronic hepatitis such a discrepancy may be important, as patients who have the ability to regenerate may also have active, aggressive cirrhosis that may compromise the results.

Ha-Kawa et al provided further studies to define the spectrum of typical time-activity curves for cirrhosis[72]. Their multicenter study indicated that this technology was reproducible in a number of settings. Using SPECT images, Hwang et al demonstrated that GSA could be used to predict the remainder of functional receptors, based on the likely size of the resection and extent of receptor populations remaining[73].

In a natural history study of hilar cholangiocarcinoma, Akaki et al recognized that occlusion of the portal vein resulted in decreased receptor numbers in the occluded segment[48]. Of more relevance to surgeons is whether this resulted in an increase of receptors in the contralateral lobe. This was more directly addressed by Nakano et al, identifying patients for transarterial chemoembolization on the basis of receptor numbers. They discovered that patients, who on the basis of their low receptor numbers at the L15 point of the GSA kinetic scan, received portal vein embolization that activity was found to increase, suggesting increased receptor numbers for the entire liver after the resection. This information is confusing, because one would anticipate an ultimate homeostatic redistribution of receptors. Their data also disclosed that a number of patients who were felt to be clearly resection candidates, and who then underwent transarterial chemoembolization, had decreases in the receptor number[61]. The trend of ICG retention and GSA scanning suggested an increase in receptor numbers when in fact we expect homeostasis at best, but on an uncertain timetable. One simple conclusion is that blood flow may alter GSA results, much as ICG retention test values are altered by changes in hepatic blood flow such as occurs in this acute situation following portal vein occlusion. A more complex analysis raises the question as to whether the mathematical model yielding receptor numbers is related to hepatocyte mass. If so, receptor expression might still vary, for reasons independent of the known hyperplasia occurring after portal vein embolization[74]. Similar derangements in GSA uptake also occur postoperatively. How this affects the time-activity curves results for GSA has been demonstrated by Tanaka et al[28]. But beyond the fact that changes occur, data regarding the specific changes resulting from specific surgical procedures are being acquired.

Kokudo et al helped elaborate on this point by demonstrating that receptor recovery after hepatic resection occurred over a number of days, and that by 21 days after resection most patients still demonstrated marked reduction in receptor concentrations[76]. Followed over time, receptor numbers appear to increase, even after 150 days postresection. Thus estimation of reserve must take into account the fact that there will be a temporary dysfunction in asialoglycoprotein endocytosis (and hepatic blood flow) that may improve with time, as long as regeneration occurs without progressive fibrosis or complicating necrosis. Changes in blood flow as estimated by dynamic curves or alternative tests have not been done in the postoperative state.

Fujioka et al, attempting to estimate functional reserve and correlate this with CT images and ICG retention, used the L15 receptor number to identify those patients with likely complications. Only 1 patient in their group of 35 patients died from liver failure [77]. Thus the predictive value to the test is limited by concomitant careful selection.

Uetake et al studied 13 patients and found that the 15-minute receptor volume correlated with an estimate of the resection volume[78]. This led to an accurate assessment of the postoperative receptor numbers, and they predicted the potential utility of GSA in the selection of patients for specific surgical procedures, based on estimates of functional remnant receptor volume[78]. Elaborating on this finding, Wakabayashi et al demonstrated that the receptor numbers could be estimated and correlated with CT volumetry[79]. And they demonstrated that, as with ICG, blood flow appeared to markedly change these values, raising the question whether simple receptor assay at 15 minutes (the L15) adequately conveys the extent of liver disease or recovery. In the most encouraging study to date, Kubo et al, employing portal vein embolization to increase hepatic reserve, demonstrated a shift in receptor numbers from right to left lobe as the liver became hyperplastic on the left[80]. This is one of the truly encouraging findings from the early literature regarding GSA.

Overall, use of GSA clinically is in its infancy. That GSA results correlate with ICG, CP, and other indices of liver function is not disputed. Whether it supplies additional information is a more complicated question to answer. It is clear from the foregoing discussion that GSA may suffer from some of the same drawbacks as ICG with regard to blood flow influences on the uptake of the agent. Virtually all of the studies discussed above correlate the GSA with another function test or the CP score. Not only are the results not correlated with outcomes, but also, the surgical results are uniformly excellent, and the small number of deaths does not provide an opportunity to correlate the test with the spectrum of postoperative liver dysfunction and failure. In addition, the simplified analyses using L15 alone may be an even greater problem for GSA analysis than for ICG, having to take into account not only functional hepatocyte mass but also blood flow which is impaired in cirrhosis.

The search for a simple number such as the L15 from the GSA scan, or the 15-minute ICG retention, ignores much important information acquired with these tests, and may do an unjust disservice to both of these methods. A simple means to summarize the acquired information and yet reflect the extent of the data acquired would be invaluable.

One of the most intriguing aspects of portal vein embolization to improve hepatic resection options in cirrhosis has gone beyond the demonstration of a volumetric change in the contralateral lobe after portal vein embolization, with and without combined hepatic artery embolization; in a limited study, improved ICG clearance has also been demonstrated[70]. It is exciting that predictable volume increases due to hyperplasia of contralateral unembolized liver parenchyma have now been followed by data convincingly demonstrating a degree of improved function—even in cirrhotics. Kubo et al's data are the most convincing evidence to date that functional improvement, not just hyperplasia, may result from portal vein embolization, and that Tc-GSA can detect this[80].

As discussed above, function studies so far have been linked to CP scores, whereas the tests should more appropriately be linked to outcomes. The potential role of these agents in evaluating resection must demonstrate that they are improvements over CP stratification, or at least additive, and do not simply duplicate predictive data acquired from the CP score.

Patient selection and resection outcomes: lessons learned from four recent series

Torzilli et al, in 1999, reported that “no mortality” liver resection for hepatocellular carcinoma was possible[81]. For preoperative selection, the three parameters that they chose to employ were: (1) the presence of ascites, (2) the serum bilirubin level, and (3) the ICG 15. The projected remaining liver volume was analyzed by computer tomographic volume averaging. For patients with projected remnant volumes under 40% or ICG 15 values of 10% to 20%, portal venous embolization was performed to increase the projected remnant volume preoperatively. One hundred seven patients underwent resection of hepatocellular carcinoma without mortality. The authors outlined a method of combining bilirubin and ascites to select patients for ICG retention studies and to suggest which patients were appropriate candidates for limited resections or for extended resections.

Analysis of their selection criteria indicate that only CP score 5 or 6 (CP Class A) patients underwent surgery. ICG 15 was used to select the very best patients (ICG 15 <10%) for extended resection (four or greater segments). All other CP Class A stratum patients underwent lesser resections as guided by the ICG 15 value. This is a notable series, with a remarkable reliance on ICG 15 for guidance and an aggressive use of portal vein embolization to attempt to increase functional reserve.

Poon et al, reporting their experience with 45 extended resections for HCC, selected CP Class A patients, who then underwent ICG 15 evaluation[82]. A combination of detailed imaging to assess remnant volume and laparoscopy with laparoscopic ultrasound, in order to detect moderate to severe cirrhosis at the time of planned resection, was employed to further select patients who might then undergo extended resection. Their group of 45 extended resection patients (greater than four segments) were compared with a group of 161 patients with four or fewer segment resections. In each group, a single death (out of three and six total in each group, respectively) occurred that could be attributed to liver failure. Two of the deaths occurred in Child-Pugh Class A patients and one occurred among 3 Child Class B patients. The authors concluded that extended resection was not indicated in Childs Class B patients. For CP Class A patients, a combination of the 15-minute ICG retention <14% for any patient, or a value between 14% and 20%, for a patient with a predicted large liver remnant volume, satisfactory results could be anticipated.

Jarnagin et al reported their experience (1991–2001) with 1803 liver resection cases for primary and metastatic disease[83]. Preoperative selection of CP Class A patients was coupled with a detailed radiologic workup. A meticulous intraoperative assessment led to a mortality of 3.1%, with only 6 of 55 deaths being linked directly to hepatic failure. The authors relied heavily on parenchyma-sparing, segmental resection. That the number of patients in the series developing liver failure was 5% (99 patients) is a testimony to the aggressiveness of the therapy. Other than the projected number of hepatic segments involved and the perioperative blood loss, no other factors reliably predicted mortality.

Redaelli et al used galactose elimination capacity with the aminopyrine breath test, in an analogous manner to the use of ICG reported above, to select 167 patients who underwent curative resection; 6 patients of 167 or 3.6% died[84]. Only 2 died of acute liver failure, and these died despite undergoing tissue-preserving resections.

The overwhelming message is that there is a considerable amount of experience-based selection in each of these series. The avoidance of greater than four-segment resections in "bad-risk" Child-Pugh Class A patients is a clear-cut goal, unless the option of portal vein occlusion is to be pursued. The estimated remnant volume—determined by preoperative imaging or by direct intraoperative assessment—and the severity of the cirrhosis determined at surgery, which is difficult to precisely quantify, appear to be of critical importance in patient selection. One question that arises from these papers is whether there is a test that provides a substantial benefit in the selection of patients for resection beyond clinical experience and the CP score. The Memorial-Sloan Kettering data reported by Jarnagin suggest that experience may play a critical, positive role in patient selection if ICG retention is not used.

Portal vein embolisation (PVE) is gaining increasing acceptance in preoperative treatment of selective patients before major liver resections. Induction of selective hypertrophy of nondiseased portion of the liver with PVE in patients either primary or secondary hepatobiliary malignancy and a small estimated functional residual volume may result fewer complications and shorter hospital stay following resection. Additionally, PVE performed in patients initially considered unsuitable for resection due to lack of sufficient normal parenchyma may add to the pool of candidates suitable for resection.

Many attempts have been made over the past few decades to classify patients with liver disease to determine their prognosis following hepatic surgery. These have included the well-known and widely used Child-Turcotte-Pugh score (CTP) as well as more obscure methods such as indocyanine green clearance. Most recently, the Model for End-Stage Liver Disease (MELD) score has gained widespread acceptance because of its use in prioritizing candidates for liver transplant. With the exception of measures of hepatic function, these scoring systems are all mathematical computations involving various laboratory values and clinical assessments and, as such, are reflections of different facets of pathology and physiology, and yield different degrees of reliability in different patient populations.

The MELD score was originally developed to predict short-term survival in patients undergoing transcutaneous intrahepatic portosystemic shunt procedures (TIPS), and has been shown to be reliable and predictive in this setting.[97-100] It is useful in assessing prognosis in patients with alcoholic hepatitis, although its superiority to CTP scores is not universally established. Furthermore, it has replaced the traditional CTP score in stratifying patients with end-stage liver disease awaiting transplantation according to guidelines adopted by the United Network for Organ Sharing in 2002.[101] Interestingly, MELD seems to predict patient and graft survival in cadaveric liver transplantation but not in living donor liver transplantation.

Extrapolating scoring schema from the originally described population is a common practice. However, we practice in an era of healthcare resource scarcity coupled with increasingly sophisticated surgical technique and critical and anesthetic care. More and more, we are in need of accurate and reliable methods for allocating scarce resources, as well as educating patients in making informed choices concerning their care. Use of MELD in patients undergoing elective liver resection is becoming more common but has not been validated.

Given the shortcomings of currently used scoring systems, there is a constant effort underway to create innovative, accurate, and clinically relevant assessment tools. However, the enthusiasm that accompanies any new system can lead to its application to situations for which it was not designed. MELD scores have been shown useful in stratifying patients with end-stage liver disease awaiting transplantation. By allocating organs to those with the highest scores rather than waiting time combined with subjective clinical assessment, improvements have been realized in short-term graft and patient survival. However, generalization to other types of hepatobiliary surgery does not seem warranted. In one analysis, ASA and CTP were both superior to MELD in predicting poor postoperative outcome. Interestingly, both CTP and ASA classification schemes involve intuitive, bedside assessment. This is especially true of the ASA classification, given its lack of explicit, defining criteria. The anesthesiologist assigning the score does so by the most general of guidelines with no specific laboratory values or mathematical calculations whatsoever. There does seem to be a role for clinical judgment and experience in predicting which patients will do well and which will not.

The most significant difference between patients undergoing TIPS procedures or awaiting liver transplantation and these patients undergoing elective hepatic resection is the variable rate of severe liver disease among the 2 groups. Presumably, all those in the first group already have severe liver dysfunction, although the exact pathogenesis does differ. The incidence of hepatic dysfunction in the second group is much lower. Although primary hepatocellular carcinoma does most often develop in the setting of cirrhosis, 91% of the patients in this series had minimal or completely no evidence of liver disease. It is true that clinical signs and symptoms of liver disease are often absent until liver disease is quite advanced. However, the clinical differences between the 2 groups are significant. This may account for the different degrees of success with which MELD is able to predict postoperative mortality and morbidity.

Complications after Liver resection:

Pleural effusion, ascites, wound and chest infections, subphrenic abscess, biliary fistulas, and hepatic insufficiency are frequent complications recorded after liver resection. Although an accurate selection of patient eligible to resection, advances in surgical techniques, and perioperative management have greatly contributed to lower the rate of perioperative deaths, stress must be put on reducing the postoperative complication rates reported to be still as high as 50%.As recently reported in the literature, there is a relationship between postoperative mortality and the presence of cirrhosis with a higher mortality rate both in alcohol abuse and patients affected by viral hepatitis B. Postoperative hepatic failure or temporary impairment liver function are the most serious complications which can occur after liver resection, in particular in cirrhotic liver: as claimed by the literature, postoperative hepatic failure, which is mainly preceded by insufficient remnant liver function, massive intraoperative bleeding followed by massive transfusion, and or postoperative septic complication, is the major cause of hospital mortality. The debate about the extension of liver resection for HCC on cirrhosis is already open and it ranges from the widest resection to obtain radical result to the limited procedure to not make the liver function worse. Recent studies revealed that a liver remnant volume lesser than 25% is associated with an increased incidence of postoperative hepatic dysfunction in patients with normal liver, but liver resection on cirrhosis must conserve about 50% of total liver volume to preserve liver function. As it has been recently reported in a series of Child–Pugh B and C, an estimated liver remnant volume (ELRV) lesser than 50% is associated with high mortality in the first year and no survival after the third year compared with an ELRV>50%. The preoperative liver remnant volume estimation led us to plan the surgical procedure in such a way as to both obtain a radical result and not make the liver function worse. This result is shown by the reduction of temporary impairment of liver function rates reported[116].

Improvements in surgical management including the use of modern devices, such as ultrasonic dissector, reduction in blood loss and blood transfusion, intermittent warm ischemia, maintenance of a low central venous pressure during hepatic transection, and shortening the procedure length have made considerable contributions to safer procedure and improved outcomes, specially in lowering postoperative complication.

Parenchymal transection is the most important stage of liver resection. The majority of intraoperative complications that affect patient outcome occur during this procedure. Many efforts have focused on achieving safe liver transection by designing the proper transection plane and developing techniques that enable performance of liver parenchymal splitting in a bloodless surgical field. Proper transection plane means that malignancies will be resected with adequate tumor-free margins and also that vascular and biliary structures, vital for the survival of the remaining liver and of the patient, will be protected from inadvertent injuries. Surgical experience and intraoperative ultrasonographic mapping of the liver allow accurate and reliable determination of the transection plane. In most series, all surgical procedures are performed after intraoperative ultrasonography which was used to define the precise extension of disease, the size of lesion, and the relationship with biliary and vascular structure. Intraoperative ultrasonography helps the surgeon to make a realistic plan of transection and guides a careful anatomical transection. Bloodless liver splitting still remains the target of various methods, and many of them incorporate some type of vascular exclusion, exploiting the liver capability to withstand continuous and intermittent warm ischemia up to 90 and 120 min, respectively. Various techniques, in addition to the old finger-fracture method, have been employed, including clamp crushing, ultrasonic dissection, hydrodissection, stapling with vascular endostaplers, heat coagulation, and sharp transection with a scalpel. The clamp crushing technique is the most popular because of its simplicity and effectiveness in controlling blood loss. This technique has been employed with or without liver vascular control. Sharp transection is used rarely; it warrants complete vascular control of the liver with either total hepatic vascular exclusion or selective hepatic vascular exclusion. Radiofrequency ablation, saline-link and radiofrequency dissecting sealer, and LigaSure have been introduced in recent years for bloodless liver transection. Intraoperative bleeding is always one of the key problems in liver surgery. It has been demonstrated that massive hemorrhage during partial hepatectomy contributes to morbidity and mortality. Besides, subsequent blood transfusion facilitates recurrence of hepatic malignancies, including both primary and secondary tumors, and decreases survival of patients. Thus, control of intraoperative hemorrhage appeared to be very important in hepatic resection. Since Pringle first reported temporary normothermic occlusion of hepatic inflow by clamping the porta hepatis in the early 20th century, the technique named Pringle maneuver has been used worldwide. But clamping-caused hepatic ischemia/reperfusion injury has been increasingly recognized with controversy on intermittent or continuous clamping in hepatic surgery. Comparison of experimental data showed that the two maneuvers lead to similar liver injury (even lightened injury in continuous clamping) in a short period, but intermittent clamping reduces hepatocellular damage in a long period of ischemia. It was demonstrated that oxygen-derived free radical played a crucial role in liver ischemia/reperfusion injury as a main mechanism of hepatic injury after clamping.Some authors have reported that liver damage due to occlusion of hepatic inflow for 40 min was reversible in rats and humans, respectively. Moreover, no significant differences were found in values between the intermittent clamping and continuous and morphological findings also suggested analogous degree of injury.

In a recent study authors have adopted Pringle maneuver during only 36.6% of liver resections and they chose an intermittent clamping that lasted for 20 min, interrupted by a restore break of 5 min, because as the liver damage due to occlusion of hepatic inflow is showed, there is no agreement on the well-timed length of occlusion when it is required. They achieved a lower incidence of intraoperative and postoperative bleeding with the introduction of Ligasure® dissector; hemostasis performed using Argon Beam associated with Ligasure® dissector leads them to carry out the surgical procedure whether with low bleeding or bloodless and they reduced the length of both Pringle maneuver and surgical procedure. As a frequent complication after hepatectomy, pleural effusion mostly affects the right liver lobe with an incidence rate of 62.9% for hilar cholangiocarcinoma and 32.01% for hepatocellular carcinoma[151 - 155].

During hepatectomy, conventional mobilization of the liver involves mechanical division of its ligamentous attachments and hemostasis with suture ligation, which usually results in damage to the integrity of lymphatic circumfluence. Compared with left hepatectomy, right hepatectomy entails extended division that causes more damage to the lymphatic path, thereby more postoperative pleural effusion occurs. Thus, to reduce the incidence of postoperative pleural effusion, it is necessary to control the division before hepatectomy. Long-term of hepatic occlusion leads to postoperative hepatic dysfunction and swelling of hepatic cell, which affects the lymphatic circumfluence. This plays a role in the development of postoperative pleural effusion. The association of the length of hepatic occlusion with postoperative pleural effusion represents injury of hepatic cell and dimension of hepatectomy. It is important to shorten the time of hepatic occlusion in an attempt to decrease the incidence of postoperative pleural effusion. When moderate or more ascites develops postoperatively, the elevated intraabdominal pressure expels the ascites into the thorax through the damaged diaphragm and adds to pleural effusion.

The incidence of biliary leakage in liver resection without biliary reconstruction was around 4–12%. The difference in the incidence of bile leakage in patients with or without liver cirrhosis is reported as not significant. Preoperative and operative factors were associated with the development of biliary complications: age, preoperative white blood cell count, left-sided hepatectomy, high-risk procedure, operation time, and intraoperative blood loss.Left-sided hemihepatectomy and central bisegmentectomy have a high incidence of postoperative bile leakage, as claimed in the literature; major hepatectomy is recorded as an independent risk factor for the development of postoperative bile leakage. It has previously been reported that the intraoperative bile leakage test cannot exclude the possibility of postoperative bile leakage because damage to the bile ducts of a small segregated segment of the liver may continue to cause bile leakage without communication with the main biliary tree. Had it occurred, the amount of bile leakage from the bile ducts of a small segregated segment of the liver would be small, and the site of bile leakage would close spontaneously in the short term. The relatively high incidence of uncontrollable leakage in patients after right-sided hepatectomy might be related to the pumping action of the right hemidiaphragm. The results of nonoperative management of bile leakage after liver transplantation and other hepatobiliary procedures are encouraging, and nonsurgical measures have become the preferred approach. The presence of bile, blood, and devitalized tissue in the dead space after hepatic resection provides the ideal environment for bacterial growth. The combination of a sudden reduction in the liver volume and development of intraperitoneal sepsis frequently results in liver failure, which has a bad prognosis. As a lower incidence of intraoperative and postoperative bleeding was achieved with the introduction of Ligasure® dissector, same result was recorded on the ground of biliary leakage: this could be explained by both a better procedure planning and a bloodless surgical procedure; the reduction of length of Pringle maneuver could help in lowering the tissue damage that support biliary leakage. Wedge resection resulted to be involved in biliary leakage development (p=0.001) probably because the lesser the procedure is anatomical the more is the probability to damage the biliary tree. In the last few years, many centres have chosen anatomical surgical procedure like segmentectomy rather than wedge resection because they believe that an anatomical resection could reduce the possibility of damage of vascular and biliary system. Most important factors, associated with arising of postoperative complications, result to be linked to surgical procedure: the extension of resection, the length of clamping, blood loss, and the amount of transfusion; when a complication has arisen, a vicious circle is established where a complication breeds and holds up other complications. A learning curve exist and the experience of the surgeons who performs surgical procedures plays an equal role as the innovation in surgical devices, advances in surgical techniques, and improving in preintra- and postoperative management. On the ground of experience from various centers, the following recommendations were made: every liver resection should be planned after intraoperative ultrasonography that helps the surgeon to make a realistic plan of transection; anatomical surgical procedure like segmentectomy should be preferred instead of wedge resection for it can prevent both vascular and biliary damage; modern devices should be used, like Argon Beam and Ligasure® dissector, to reduce the incidence of both intraoperative and postoperative bleeding and biliary leakage[116].

Hospital Volume and Hepatectomy

The empirical relationship between high hospital volume and improved outcomes is well established for several high-risk surgical procedures. Patients undergoing surgery at low-volume hospitals had a 3-fold increased risk of in-hospital mortality after adjusting for differences in patient characteristics. In addition, we demonstrated that patients who have surgery at low-volume hospitals are at risk for several specific postoperative complications. These include life-threatening complications, such as acute renal failure, pulmonary failure, reintubation, and nosocomial pneumonia. After entering these complications into the multivariate model, hospital volume was no longer statistically significant, suggesting that the mechanism of improved outcome at high-volume hospitals may be fewer postoperative complications[117].

Several population-based studies have demonstrated improved outcomes for patients who undergo hepatic resection at high-volume vs low-volume centers. Begg et al[120] merged data from the Surveillance, Epidemiology, and End Results database with clinical data for Medicare patients and studied the effect of volume on outcomes for several high-risk surgical oncology procedures. This study showed a significant reduction in 30-day mortality associated with high-volume hospitals after hepatic resection for malignancy (5.4% at low-volume vs 1.7% at high-volume centers). Two studies using state discharge databases from Maryland and California also demonstrated decreased mortality at high-volume centers. Choti et al[119] reviewed 606 liver resections done in Maryland between 1990 and 1996. High-volume hospitals in Maryland had an in-hospital mortality rate of 1.5% vs 7.9% at low-volume hospitals (P<.001). Using the discharge database in California, Glasgow et al studied the influence of hospital volume on outcomes of hepatic resection for hepatocellular carcinoma. For 507 patients, risk-adjusted operative mortality was 22.7% at low-volume centers and 9.4% at high-volume centers (P =.002). The latter study from California was exclusively investigating hepatocellular carcinoma, which represents a higher-risk patient population due to the frequency of underlying liver disease and the large extent of resection necessary to obtain negative margins. The relationship of hospital experience to both clinical and economic outcomes is well known. Well-designed studies have shown significant volume-outcome effects for several high-risk surgical procedures, including hepatectomy, esophagectomy, pancreaticoduodenectomy, abdominal aortic aneurysm repair, coronary artery bypass grafting, and many others[118-120]. The health policy implications of this volume-outcome relationship are important. Many policymakers have suggested regionalizing complex surgery to high-volume centers of excellence, and some health policy initiatives are currently underway. Currently, the best surrogate for quality of care at different hospitals is hospital experience. To concentrate patient care in the hands of high-quality (high-volume) hospitals, the Leapfrog group has set minimum volume standards that institutions must meet to provide those services to their patients. Birkmeyer and colleagues[121] estimated that almost 2600 deaths after surgery could be avoided in the United States each year by "universal adoption" of this evidence-based hospital referral policy.

Regionalization, however, may not be an acceptable solution for all patient populations. Some patients may prefer to undergo surgery at local institutions, even if confronted with a higher risk of perioperative mortality. In rural areas, referring patients to higher-volume centers may be physically or financially unfeasible. The estimate by Birkmeyer et al[121] of the benefits of regionalization included only urban areas. Good outcomes can be achieved in these select low-volume centers. For example, a recent series of 18 liver resections (4 trisegmentectomies, 4 lobectomies, 4 segmentectomies, and 6 wedge resections) in a community hospital in Maryland reported a 0% mortality rate. This experience may be anecdotal but it suggests that hospital volume may not be the best surrogate for quality. Further studies are needed to elucidate the factors that explain the volume-outcome relationship. The hospital volume variable is complex and likely represents several structure and process differences between high- and low-volume hospitals. Isolating these differences will allow for changes at low-volume hospitals that will improve outcome. Some evidence exists that demonstrates the importance of intensive care unit (ICU) physician and nurse staffing in predicting outcomes after complex surgery. Having daily rounds by an ICU physician was associated with a 4-fold reduction in mortality and a decreased risk of complications after hepatic resection in one recent study, and has also been demonstrated for other high-risk surgical procedures. In addition, having "more nurses" (1 ICU nurse to 1 or 2 patients) in the ICU at night was associated with fewer pulmonary complications and less resource use after hepatic resection. These differences in ICU structure may contribute to differences in complications between high- and low-volume centers, which can be changed to improve outcomes at lower-volume centers. [122-127]

PATIENTS AND METHODS

During a period from August, 2004, to March, 2007, 40 consecutive patients underwent elective hepatic resection for benign or malignant hepatobiliary diseases at the Department of Surgical Gastroenterology, Government Stanley Hospital, Chennai, Tamilnadu. The hepatectomies were performed by a surgical team specialized in hepatobiliary surgery.

Preoperative Assessment

All patients had ultrasonography and contrast computed tomography (CT) scan or magnetic resonance imaging to evaluate the liver or biliary pathology. Assessment of liver function was based on Child's classification, liver biochemistry, and coagulation profile. In patients with hepatocellular carcinoma (HCC), preoperative biopsy is not routinely performed if the lesion is operable. CT volumetry was used to aid assessment of liver function reserve.

Operative Techniques

Patients undergoing hepatectomy were generally explored through a bilateral subcostal incision with vertical midline extension. In selected patients with a large right lobe tumor or a small tumor located at the superior and posterior part of the right liver, a thoracoabdominal approach was used.[22] Staging laparoscopy have been used with increasing frequency to assess the extent of tumors and to assess the severity of any cirrhosis and size of liver remnant.[23] After laparotomy, intraoperative ultrasound was routinely performed to detect any lesions in the contralateral lobe, any tumor invasion of portal vein or hepatic veins, and to define the relationship between the tumor and major intrahepatic vessels. Parenchymal transection was performed using the finger-fracture technique, Kelly Clyssis, ultrasonic dissector (CUSA). In some cases of right hepatectomy for a large tumor that made mobilization of the right lobe difficult, parenchymal transection was performed without premobilization of the liver and extra hepatic control of the right hepatic vein (anterior approach).[24] The hepatic duct was isolated and ligated or sutured at the time of hepatic transection. We have routinely mobilized the liver and isolated the portal structures and hepatic veins extra hepatically or hepatic veins were isolated during hepatic transection on the left side. Intermittent Pringle maneuver was not used routinely, with increased experience in recent years, Pringle maneuver was used only when significant bleeding was encountered. Instead, more attention was paid to lowering of the central venous pressure to below 5 cm H2O to reduce venous bleeding during transection. Total vascular exclusion was not performed in any patients. Meticulous attention was paid to the preservation of function in the remnant liver by avoiding prolonged rotation, hypoxic injury, or venous congestion due to overloading of circulation. After transection, bile leakage test was performed using normal saline injection via a cystic duct cannula, and any leakage site was carefully repaired with fine sutures. Blood transfusion was initiated when the hemoglobin level fell to below 8 g/dL or when there was a hemodynamic instability. We use fresh frozen plasma during or after operation. An abdominal drain was placed almost routinely after hepatic resection.

Postoperative Care

All patients with major hepatic resection were monitored in the intensive care unit in the immediate postoperative period. The need for postoperative mechanical ventilation was determined by the anesthetists. Pain control was provided by intravenous pentazocine injection if the patient needed mechanical ventilation; otherwise, pain was controlled by on demand epidural analgesia through an epidural catheter placed preoperatively. A broad-spectrum antibiotic was given for at least 5 days, and intravenous albumin was given for cirrhotic patients with hypoalbuminemia. Oral feeding was started when the bowel sounds returned.

Data Collection and definitions

To analyze the trends in perioperative variables and outcome of hepatectomy in our institution over the 3 -year study period, Pre-, intra-, and postoperative data were recorded prospectively in a computerized database. Histopathological data including status of underlying liver (normal, chronic hepatitis, cirrhosis) were also collected. The types of hepatic resection were described according to the terminology recommended by the International Hepato-Pancreato-Biliary Association.[25] Concomitant procedure was defined as any extrahepatic organ resection, portal lymphadenectomy, or extrahepatic biliary resection and reconstruction. Thoracotomy and cholecystectomy were not considered as additional extrahepatic procedures. Hospital mortality was defined as any death that occurred during the same hospital admission for the hepatic resection.

Statistical Analysis

Continuous variables were expressed as median and interquartile range and compared using Mann-Whitney *U* test. Categorical variables were compared by the _2 test with Yates' correction or Fisher exact test where appropriate. Multivariate analyses of risk factors of morbidity and mortality were performed using a binary logistic regression model. All statistical analyses were performed using statistical software (SPSS 9.05 for Windows, SPSS, Inc, Chicago, IL). Results were considered significant at $P < 0.05$.

RESULTS

During the study period, 23 men and 17 women underwent hepatectomy for benign or malignant hepatobiliary diseases **(Table 1)**. The most common indication was HCC, which accounted for 72% of all hepatectomies. Two patients underwent hepatectomy for metastatic disease 1 colorectal and 1 noncolorectal (renal cell carcinoma).The most common benign indication was for hemangioma. One patient underwent major hepatectomy for persistent bronchobiliary fistula and 1 for a rare benign fibrous tumour of the liver.

Preoperative Variables

Age, gender, presence of comorbid illness, presence of cirrhosis, presence of thrombocytopenia (platelet value < 150 X 10^9/ L), hypoalbuminemia (Serum albumin < 40 gms/L), hyperbilirubinemia (S.bilirubin > 2mgm/L), prothrombin time (> 12 seconds), elevated serum creatinine (>1.3 mgm %) were the preoperative variables that were considered. **Table 2** shows the preoperative variables. The mean age of patients who underwent hepatectomy was 47.1 years [41.83 – 52.32]; the median age was 49 years [14 – 82 years]. There were 23 males and 17 females. 37.5% of patients had comorbid medical conditions. The most common comorbid condition was cardiovascular disease, followed by diabetes mellitus, chronic respiratory disease , and chronic renal disease. 11 out of 40 patients were cirrhotics (27.5%) and the remaining had normal liver. 36/40 patients had Serum albumin < 40gms%, mean prothrombin time was 16.2 seconds [11 – 37 seconds], thrombocytopenia was seen in 31/40 patients. Elevated serum creatinine was seen in only 5% of patients.

Operative Variables

Of the 40 patients, 31 (77%) underwent major hepatic resection, whereas the other 9 patients (13%) underwent minor hepatic resection of 2 or fewer segments. **Table 3** depicts the frequencies of various types of hepatectomy. Most of the hepatectomies were anatomic resections, with only 5% being non anatomical resections. Extended right or classical right hepatectomy was performed in a substantial proportion of patients. Concomitant extra hepatic procedures were performed in 13 patients (32.5%). These procedures included partial excision of the diaphragm (n _ 4), hepatico jejunostomy with

Table 1

Indications of Liver resection

Malignant disease	**34(85%)**
I Primary liver malignancy	
1. Hepatocellular carcinoma	29(72%)
2. Intrahepatic cholangiocarcinoma	1(2.5%)
II Metastatic liver malignancy	
3. Colorectal	1(2.5%)
4. Others	1(2.5%)
III Extrahepatic Cholangiocarcinoma	
5. Cholangiocarcinoma	2(5 %)
Benign disease	**6(15%)**
I Hemangioma	2(5%)
II Adenoma	1(2.5%)
III Persistent Bronchobiliary fistula	1(2.5%)
IV Benign fibrous tumour	1(2.5%)
V Others	1(2.5%)

Table2

Pre operative variables

Age (Median)	**49 (14 - 82) years**
Gender (M:F)	**23:17**
Presence of comorbid illness	**15(37.5%)**
Cirrhotic liver	**11(27.5%)**
Thrombocytopenia (Plt < 150 X 10^9)	**31(77.5%)**
Hypoalbuminemia (S.albumin < 40gms/L)	**36(90%)**
Hyperbilirubinemia (S.Bilirubin >2mgm/dl)	**5(12.5%)**
Prothrombin time (> 12 seconds)	**16.2(11 - 37)**
Elevated Serum creatinine (> 1.3 mgm/dl)	**2(5%)**

or without excision of the bile duct (n _ 4), adrenal gland (n _ 8), lung (n _ 1), Some patients had more than 1 extrahepatic procedure. Additional ablation of liver tumors in the contralateral lobe was performed in 2 patients, including radiofrequency ablation in 2 patients in group II. **Table 4** shows operative variables. The use of Pringle maneuver was in 45% of patients. The abdominal drainage was used in majority of patients (95%). Average operative blood loss was 342 (50 – 2000) ml. Perioperative blood transfusion was needed in 18/40(45%) patients. Average volume of blood transfusion required was 1.47 (0 - 6) units. Volume of fresh frozen plasma transfusion required was 5.55(0 – 18) units.

Perioperative Outcome

The overall morbidity and hospital mortality of the 40 patients were 40% (n _ 16) and 5 % (n _ 2), respectively. The causes of death were hemorrhage with uncontrolled coagulopathy in 1 patient and hepatic failure in 1 patient. The hospital mortality rate was higher after hepatic resection for malignant disease than after hepatic resection for benign disease (5.8% versus 0%), and the hospital mortality rate in cirrhotic patients was equal to noncirrhotic patients. When stratified according to the type of hepatectomy, the hospital mortality was observed in 1 patient with extended right hepatectomy and 1 patient with extended left hepatectomy. The hospital mortality rates of segmentectomy and nonanatomical resection was 0% while that of major resections was 2/31(11%). **Table 5** shows the perioperative outcomes. The mean ICU stay was 3.3 (1 – 14) days; post operative mechanical ventilation was needed in 12/40(30%) of patients. Post operative day of resumption of enteral feeds was 4.3(0-10) days. The mean hospital stay was 16.2 (10 – 40) days. Morbidity was observed in 16/40 patients and the various complications and their frequency are listed in **Table 6**.

Table 3

Types of hepatic resections

Major resections	**31(89%)**
Rt Hepatectomy	16(40%)
Rt Extended Hepatectomy	6(15%)
Lt Hepatectomy	6(15%)
Lt Extended Hepatectomy	2(5%)
Central Hepatectomy	1(2.5%)
Minor resections	**9(11%)**
Bisegmentectomy	
Lt lateral sectionectomy	5(12.5%)
Rt Posterior sectorectomy	1(2.5%)
Other resection involving 2 segments	1(2.5%)
Unisegmentectomy	0
Non anatomical resection	2(5%)

Table 4

List of Operative variables

Extent of Hepatic resection	
Major	**31(77.5%)**
Minor	**9(22.5%)**
Concomitant extra hepatic procedure	**13(32.5%)**
Use of Pringle's Maneuver	**18(45%)**
Use of abdominal drain	**38(95%)**
Operative Blood loss, ml	**342.5(50 - 2000)**
Perioperative blood transfusion	**18(45%)**
Intra operative hypotension	**13(32.5%)**
Volume of Blood transfusion, units	**1.47(0 - 6)**
Volume of Fresh frozen plasma, units	**5.55(0 - 18)**

Table 5

Perioperative Outcomes

ICU care unit stay, days	**3.3(1 – 14)**
Post operative mechanical ventilation	**12(30%)**
Post operative parenteral nutrition	**8(20%)**
Post operative day of resumption of oral feeding, days	**4.3(1-10 days)**
Hospital stay, days	**16.2(10 – 40)**
Overall morbidity	**16(40%)**
Hospital mortality	**2(5%)**

Among the surgical complications, wound infection and wound dehiscence were the most common complications observed and contributed to morbidity. Bile leak was observed in 3/40 (7.5%) of patients. Transient ascites, liver failure, pleural effusions were the medical complications that were noted at a frequency of 30%, 7.5% and 7.5% respectively.

Three patients had liver failure which was managed medically and of the three two patients survived and one died.

Table 6

Complications

Surgical Complications	**no(%)**
Bile collection	**3(7.5%)**
Intraabdominal abscess	**1(2.5%)**
Post operative hemorrhage	**1(2.5%)**
Wound infection	**6(15%)**
Wound dehiscence	**3(7.5%)**
Medical Complications	
Liver failure	**3(7.5%)**
Ascites	**12(30%)**
Variceal bleeding	**0**
Broncho pneumonia	**1(2.5%)**
Pleural effusion	**3(7.5%)**
Renal failure	**1(2.5%)**

RISK FACTORS FOR MORBIDITY AND HOSPITAL MORTALITY

Univariate analyses

Table 7 shows the influence of preoperative and operative variables on morbidity and hospital mortality of the 40 patients by univariate analysis. Concomitant comorbid illness, hyperbilirubinemia, hypoalbuminemia, prolonged prothrombin time, major hepatic resection, concomitant extra hepatic procedure, Pringles maneuver, blood loss of more than1 L, need for perioperative blood transfusion and fresh frozen plasma more than six units and presence of intraoperative hypotension were associated with increased morbidity, whereas presence of comorbid illness, prolonged prothrombin time, concomitant extra hepatic procedures and operative blood loss of more than 1 litre, was associated with increased hospital mortality.

Multivariate analyses

Multivariate analyses of risk factors for morbidity and hospital mortality, respectively, were performed by entering the significant factors identified in univariate analyses into a logistic regression model. None of the patients attained statistical significance as independent factors for predicting morbidity and mortality **(Table 8).**

Table 7

Risk factors predicting morbidity and mortality – Univariate analyses

	Morbidity %	P Value	Mortality %	P value
Gender				
Male (n= 23)	13 (56)	0.18	2 (8)	0.21
Female (n= 17)	6 (35)		0	
Age				
≤ 70years (n=37)	17(45)	0.48	2(5)	0.68
> 70 Years (n= 3)	2(66)		0	
Co morbid Illness				
No (n= 25)	6(24)	**0.00**	0	**0.05**
Yes (n= 15)	13(86)		2(13)	
Diagnosis				
Benign (n= 6)	1(16)	0.12	0	0.58
Malignant (n= 34)	18(52)		2(5)	
Cirrhotic liver				
No(29)	13(44)	0.58	1(3)	0.47
Yes(11)	6(54)		1(9)	

Hyper bilirubinemia				
No(29)	9(31)	**0.007**	1(3)	0.46
Yes(11)	10(90)		1(9)	
Hypo albuminemia				
No (n= 28)	8(28)	**0.00**	1(3)	0.52
Yes (n= 12)	11(91)		1(9)	
Prothrombin time > 12s				
No (n= 28)	11(39)	**0.00**	0	**0.02**
Yes (n= 12)	8(66)		2(16)	
Thrombocytopenia				
No (n=9)	3(33)	0.33	0	0.43
Yes (n=31)	16(51)		2(6)	
S. Creatinine (> 1.3 mg/L)				
No (n= 38)	17(44)	0.12	2(5)	0.73
Yes (n= 2)	2(100)		0	
Extent by Resection				
Major (n= 31)	18(58)	**0.01**	2(6)	0.43
Minor (n= 9)	1(11)		0	
Extra hepatic procedure				
No (n=27)	8(29)	**0.001**	0	**0.04**
Yes (n=13)	11(84)		2(15)	
Pringle maneuver				
No (n= 21)	5(23)	**0.001**	0	0.11
Yes (n= 19)	14(73)		2(10)	

Bl. Loss				
< 1 litre (n= 26)	7(26)	**0.001**	0	**0.05**
≥ 1 litre (n= 14)	12(85)		2(14)	
Blood transfusion				
No (n= 22)	4(18)	**0.001**	0	0.11
Yes (n= 18)	15(83)		2(11)	
Fresh frozen plasma (≥ 6 units)				
No (n= 23)	6(26)	**0.002**	0	0.09
Yes (n= 17)	13(76)		2(11)	
Intra op Hypotension				
No (n= 27)	8(29)	**0.001**	0	0.58
Yes (n= 13)	11(84)		2(15)	

Table 8

Risk factors predicting morbidity and mortality – Multivariate analyses

Parameter	**Significance**	**Risk Ratio (95% confidence interval)**
Extra hepatic resection	0.03	12.5 (1.20 – 12.9)
Pringles Maneuver	0.54	2.05 (0.20 – 20.9)
Blood Loss	0.69	0.37 (0.01 – 54)
Blood Transfusion	0.07	14.9 (0.78 – 285)
FFP Transfusion	0.56	2.1 (0.16 – 28)
Intra op Hypotension	0.87	0.87 (0.01 - 17)

DISCUSSION

Liver resections are increasingly performed as a standard treatment of various hepatobiliary diseases. However, there were few contemporary studies of the perioperative outcome of hepatic resection.[3-5] In a study of 747 hepatectomies Belghiti et al[3] demonstrated a operative mortality of 1% in patients with normal liver, but the operative mortality rate was 8.7% in cirrhotic patients. Jarnagin et al[4] reported a series of 1803 patients with hepatic resection and demonstrated a significant improvement in the perioperative outcome over the study period, which was attributed to the increased use of parenchymal preserving segmental resections and decrease in the number of hepatic segments resected. More recently Imamura et al reported zero mortality after hepatic resection in a series of 915 patients. The authors emphasized the importance of case selection, and they adopted a strict selection in terms of liver function reserve. The current study demonstrated that improved perioperative outcome could be achieved even when the indications of hepatectomy were extended to More high-risk patients with borderline liver function reserve, advanced age ,and comorbid medical illnesses.

Our patient population was characterized by a high proportion of patients with HCC.

In contrast, in the study of Jarnagin et al, metastatic colorectal cancer accounted for 62% of the indications for hepatectomy, whereas cirrhosis or fibrosis was present in only 8.8% of the patients. Hepatic resection in cirrhotic liver is technically more challenging than resection in normal liver, with increased risk of bleeding, septic complications, and postoperative liver failure. Several authors have emphasized the importance of strict selection in terms of liver function reserve in ensuring favorable perioperative [5,11,31]Outcomes in patients with chronic liver disease. ICG clearance is a commonly used test of liver function to aid selection of patients for hepatectomy. In the study by[5] Imamura et al, only patients with ICGR-15 of less than10% were offered right hepatectomy or extended hepatectomy. The use of such a strict selection criterion was considered by the authors to be a major factor for the excellent result of zero mortality in their series. Poon et al has offered major hepatectomy to patients with less favorable liver function reserve. Before 1997, major hepatic resection was offered to patients with ICGR-15 of less than 14%. In recent years, they have adopted an even more liberal selection criterion and offered right hepatectomy or extended hepatectomy to patients with[22]ICGR-15 up to 20%. Their aggressive approach was partly driven by the improving survival results that they have observed in hepatic resection for HCC, even for large HCC that [22,32] required extended hepatectomy. Excluding living donors with normal liver undergoing donor hepatectomy for liver transplantation, the proportion of patients with resection of 2 Or more Couinaud segments were 80. 2% in their series, as[5] Compared with 27.3% in the study by Imamura et al. In fact, the proportion of major hepatic resection was not the highest in this series compared with the other 3 large series[3-5] of hepatectomy recently reported in the literature.

While major hepatic resection was a risk factor for hospital mortality, the hospital mortality of 5% after major hepatic resection is acceptable. Cirrhosis was not associated with increased morbidity and hospital mortality in both univariate analyses and multivariate analyses. And, thrombocytopenia was not a significant risk factor in both univariate and multivariate analyses of both morbidity and hospital mortality, and hypo albuminemia was another risk factor for hospital mortality and morbidity in univariate analysis. Jarnagin et al also found that preoperative thrombocytopenia was an independent risk factor of mortality after hepatic resection, and hypo albuminemia was a risk factor for morbidity. In the study by Poon et al , majority of patients had higher hypo albuminemia and thrombocytopenia, yet the operative morbidity and hospital mortality had decreased. Presumably the adverse effects of hypo albuminemia and thrombocytopenia were compensated by the improvement in surgical techniques and perioperative care.

While our experience is more concentrated on hepatic resection for HCC, a more aggressive surgical approach has also been extended to other hepatobiliary cancers. Recent studies from other groups have demonstrated improved survival with aggressive surgical approach in other hepatobiliary malignancies such as colorectal liver metastasis and hilar cholangiocarcinoma.[33–35] Resection of these malignancies often requires concomitant extrahepatic procedures such as synchronous colonic resection or extrahepatic biliary resection and reconstruction. Extrahepatic biliary procedures are also required for some benign indications such as hepatolithiasis.[36] While previous studies found that extrahepatic procedures increased the risk of mortality in patients undergoing hepatectomy,[3,4] in our experience, extrahepatic procedures were associated with increased morbidity and increased mortality. The capability to perform hepatectomy combined with major extrahepatic procedures safely should help to expand the role of hepatic resection to more complicated hepatobiliary diseases. Two strategies have further expanded the indications for hepatic resection. One is preoperative portal vein embolization to induce hypertrophy of liver remnant in patients with inadequate liver function reserve and small liver remnant volume. This strategy can be employed not only in patients with normal liver but also in selected patients with chronic liver disease or biliary obstruction from extrahepatic biliary malignancies.[35,37] The other strategy is the use of radiofrequency ablation in combination with hepatic resection, which can be used to treat multiple bilobar malignancies when it is anatomically not feasible or too risky to encompass all the lesions by hepatic resection alone.[38]

In addition to the liver function reserve, advanced age and comorbid illnesses are other pre-existing host conditions that sometimes preclude patients from hepatic resection. Some previous studies have reported that advanced age was a significant risk factor for morbidity or mortality after hepatic resection,[4,14,20,39] and comorbid illnesses such as cardiovascular disease and diabetes mellitus have also been reported to be significant risk factors.[11,39,40] However, recent studies from Hong Kong group and others have demonstrated that advanced age or comorbid illnesses may not adversely affect the outcome of hepatic resection, provided that careful preoperative assessment and meticulous perioperative management were executed.[41–43] Hence, in recent years, we have become more liberal in offering hepatic resection to elderly patients and patients with comorbid illnesses. In this study, advanced age was not associated with significantly increased morbidity or mortality. While associated comorbid illness was associated with higher morbidity and mortality. Nevertheless, we would like to emphasize that careful preoperative case selection and meticulous postoperative management in liaison with the anesthetists and the relevant specialist physicians are essential to achieve favorable outcome in elderly patients and patients with comorbid illnesses. The operative morbidity and hospital mortality have been reduced in recent years the proportions of elderly patients and patients with comorbid illnesses, in particular cardiovascular disease, have increased significantly. Of the medical complications, there is a significant reduction in the incidence of respiratory complications. Better postoperative pain control with the use of patient-controlled analgesia probably has played an important role in reducing respiratory complications. With the aging population worldwide, the survival benefit of hepatic resection for malignant diseases in elderly patients is expected to increase, and hence hepatic resection is going to play an increasingly important role in this group of patients. A previous study on HCC by Hong Kong group showed a similar survival benefit from hepatic resection in elderly patients compared with younger patients.[41] While we advocate that the role of hepatectomy can be expanded in elderly patients and patients with comorbid illnesses such as diabetes mellitus and cardiovascular diseases that are under control, we caution against hepatic resection in patients with impaired renal function, because elevated serum creatinine level was a significant risk factor of mortality in many studies though it was not an observation in our study. A previous study on extended hepatic resection has also identified elevated serum creatinine level as a risk factor of postoperative mortality.[44]

Jarnagin et al[4] observed that the improved perioperative outcomes of hepatic resection in their study were largely the result of a decline in the number of liver segments resected. In contrast, in our study, the overall improvement in perioperative outcome over the study period was mainly ascribed to the reduced mortality and morbidity in patients undergoing major hepatic resection. Over the study period, there have been substantial changes in the surgical technique of hepatic resection and perioperative management. It is difficult to attribute the reduced operative morbidity and hospital mortality to a specific factor. Among the risk factors of morbidity and mortality in the Univariate analyses, perioperative blood transfusion was a risk factor for morbidity and when blood transfusion is reduced with modern techniques of parenchymal transection the peri operative outcomes of hepatectomy can be considerably improved. Several changes in the surgical technique over the years, including the use of ultrasonic dissection instead of the finger-fracture technique, the adoption of a low central venous pressure during hepatic transection and the use of a vascular stapler for control of hepatic veins, together with the increased experience of the surgeons, have all contributed to the reduction in operative blood loss. A notable change in the surgical technique in recent years is the reduced use of Pringle maneuver. Although many authors have previously demonstrated in a randomized trial that Pringle maneuver was effective in reducing blood loss during hepatic transection,[26] Fan et al has also observed a time constraint in the total duration of Pringle maneuver that the liver could tolerate,[45] which could sometimes lead to a hasty transection and hence more bleeding. With increased experience, we found that hepatic transection could be performed with low blood loss even without the Pringle maneuver. The absence of a time constraint from Pringle maneuver allows the surgeon to control each bleeding point precisely before continuing with the transection. Change in attitude toward the use of Pringle maneuver is partly influenced by growing experience in living donor hepatectomy, in which portal clamping is never applied. In a study by Poon et al of the 163 living donor hepatectomies performed without Pringle maneuver in their unit including 129 patients with right lobe donation, only 1 patient required perioperative blood transfusion, and there was no hospital mortality. In recent years, most of the hepatic resections, including those on cirrhotic liver, were performed without Pringle maneuver, and operative blood loss and the requirement for blood transfusion were on the decreasing trend. Perioperative blood transfusion could increase perioperative morbidity and mortality by causing immune suppression, and it has also been shown to adversely affect the long-term survival after hepatic resection for HCC or colorectal metastasis[46, 47]. The achievement of zero blood transfusion rates should be a common goal of all surgeons performing hepatic resection.

In our study by univariate analysis concomitant comorbid illness, hyperbilirubinemia, hypoalbuminemia, prolonged prothrombin time, major hepatic resection, concomitant extra hepatic procedure, Pringles maneuver, blood loss of more than1 L, need for perioperative blood transfusion and fresh frozen plasma more than six units and presence of intraoperative hypotension were associated with increased morbidity, whereas presence of comorbid illness, prolonged prothrombin time, concomitant extra hepatic procedures and operative blood loss of more than 1 litre, was associated with increased hospital mortality. This was in consistence with multiple studies from various centers. In multivariate analyses none of the parameters attained statistical significance as independent factors for predicting morbidity and mortality.

This is probably because the number of patients included in the study was small and for a good multivariate analysis the minimum number of patients required is at least 50.

CONCLUSION

This study demonstrated that perioperative outcome has improved despite extending the indication of hepatectomy to more high-risk patients. Hence, the role of hepatectomy in the management of benign and malignant hepatobiliary diseases can be expanded.

Concomitant comorbid illness, hyperbilirubinemia, hypoalbuminemia, prolonged prothrombin time, major hepatic resection, concomitant extra hepatic procedure, Pringles maneuver, blood loss of more than1 L, need for perioperative blood transfusion and fresh frozen plasma more than six units and presence of intraoperative hypotension were associated with increased morbidity, whereas presence of comorbid illness, prolonged prothrombin time, concomitant extra hepatic procedures and operative blood loss of more than 1 litre, was associated with increased hospital mortality.

Reduced perioperative blood loss hence reduction in transfusion requirement is a main contributory factor for the improved outcome, and further effort should be directed toward improving surgical techniques to achieve bloodless hepatic resection.

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